CBER Update: Advertising and Promotional Labeling Branch (APLB)

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RAPS Advertising, Promotion & Labeling Conference 2-3 June 2005





- Overview of APLB
- Looking Back...an Enforcement Review
- Practical Advice
- Looking Ahead...



Creativity never ceases to amaze!

U.S.: No billboards in space

WASHINGTON (Reuters) -- The U.S. government does not want billboards in space.

The Federal Aviation Administration proposed Thursday to amend its regulations to ensure that it can enforce a law that prohibits "obtrusive" advertising in zero gravity.

"Objects placed in orbit, if large enough, could be seen by people around the world for long periods of time," the FAA said in a regulatory filing.

Currently, the FAA lacks the authority to enforce the existing law.

For instance, outsized billboards deployed by a space company into low Earth orbit could appear as large as the moon and be seen without a telescope, the FAA said. Big and bright advertisements might hinder astronomers.

"Large advertisements could destroy the darkness of the night sky," regulators said.

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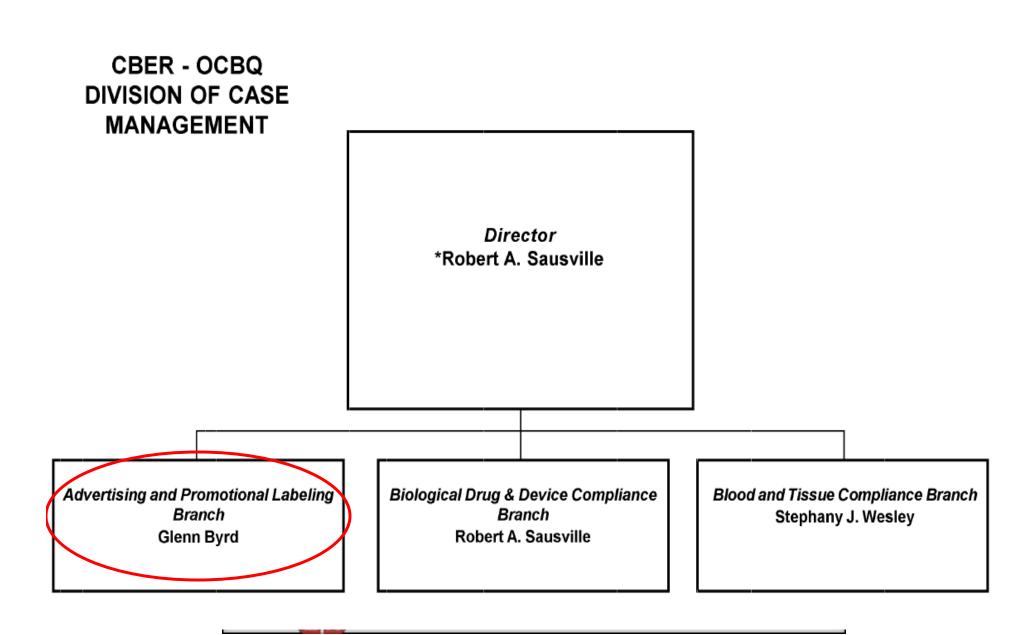
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Looking Back...

An Enforcement Review



APLB Advisory Actions 6/04 - 5/05

- Untitled Letters three (3) issued
 - Vivotif Berna Biotech (6/04)
 - Helixate FS Bayer HealthCare (8/04)
 - WinRho Cangene Corp. (1/05)

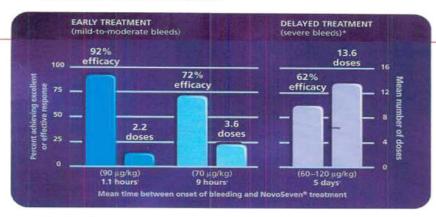
APLB Advisory Actions 6/04 - 5/05

- Warning Letters eight (8) issued
 - □ Engerix-B, Havrix, Twinrix GlaxoSmithKline Biologics (7/04)
 - NovoSeven Novo Nordisk Pharmaceuticals (8/04)
 - Rhophylac ZLB Bioplasma (9/04)
 - Zemaira Aventis Behring (10/04)
 - □ DigiFab Protherics, Inc. (11/04)
 - Nabi-Hb Nabi Biopharmaceuticals (1/05)
 - ☐ Flebogamma Instituto Grifols (3/05)
- All CBER Enforcement letters are posted at: www.fda.gov/cber/efoi/adpromo.htm

For the treatment of bleeding episodes in hemophilia A or B patients with inhibitors to FVIII or FIX

NovoSeven®: Clinical advantages with early treatment

3 NovoSeven® studies of treatment for intramuscular bleeds¹⁻³



* NovoSeven® used as salvage therapy.

Three separate studies analyzed a total of 245 peripheral intramuscular bleeding episodes. Time from onset of bleed until first treatment, dosage, number of doses, and responses were recorded for each study. Enrolled subjects had hemophilia A or B with inhibitors (several patients in the late treatment study had acquired inhibitors; several patients in the early treatment study (treatment after 9 hours) had hemophilia without inhibitors).

"...data suggest that in >90% of cases...
early administration of rFVIIa achieves
haemostasis after 1 to 3 injections. In more
than 90% of responders, haemostasis is
maintained for at least 24 h."

-Key NS et al, 1998

 Early administration of coagulation factor in patients with bleeding episodes can reduce pain and the risk of arthritis and permanent disability⁴







Rhophylac

Rhophylac Rh.(D) Immune Globulin Intravenous (Human)

Purity delivered

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MEDICAL PROFESSIONALS

PATIENTS

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NEWS & EVENTS

ZLB Behring

Page 1 of 1

The Rhophylac® Advantage

Your doctor has prescribed Rhophylac* because of its unique benefits:

- Rhophylac* is convenient to use because it can be given 2 ways through an
 intravenous (IV) line, which many patients find more comfortable, or by
 injection into a muscle (IM)
- Rhophylac[®] is a very safe, highly pure product, prepared at a modern, state-of-the-art facility
- Rhophylac* is thimerosal-free, mercury-free, and latex-free

If you are among the one in ten mothers who is Rh-negative, your doctor will talk to you about a serious but treatable condition, known as hemolytic disease of the newborn (HDN), that could impact the health of your baby and your ability to have more children in the future. It will be very important for you to consider taking Rhophylac[®], a special treatment that can help protect you and your baby from harm.

Rhophylac[®] is a specially prepared product given to women with Rh-negative blood during pregnancies when the father has Rh-positive blood. It is generically known as Rho(D) Immunoglobulin Intravenous (Human), or "Rhīg" for short. Like all Rhīg therapies, Rhophylac[®] is made from human plasma; Rhophylac[®] is made from human plasma; Rhophylac[®] is designed to prevent HDN by removing the Rh-positive blood cells that can cause a woman's immune system to develop antibodies. It is also used in mismatched blood transfusions.

Although all RhIg products are given as shots, Rhophylac[®] is the only RhIg made by the ChromaPlus process. Not only does ChromaPlus allows for administration options that make Rhophylac[®] more comfortable and faster acting than a traditional RhIg shot, but it also ensures that the RhIg is highly pure and unparalleled for safety.

This site is currently under construction and new tools and resources are being added every day. Please check back again soon!

As with all plasma-derived products, Rhophylac® may contain infectious agents such as viruses that can cause disease. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is considered extremely remote.

For more information, please see full Prescribing Information and List of References.

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PATIENTS

Patients Overview

Product Information

WinRho SDF®

Plasma Products

Vision, Mission and

PhosLo®

Nabi-HB®

Aloprim™

Values



* ABOUT US

· PIPELINE

* PRODUCTS

POWERING THE IMM

Page 1 of 1

PATIENTS Patients Overview Product Information PhosLo® Nabi-HB® WinRho SDF® Aloprim ™

Plasma Products

Vision, Mission and

Values



Patients

Welcome to Nabi Biopharmaceuticals' patient area. Nabi Biopharmaceuticals specializes in developing biopharmaceutical products that address serious, unmet medical needs in the areas of infectious, autoimmune and addictive diseases.

This patient area is designed to help you learn more about the company's four marketed products:

- PhosLo® (calcium acetate) Gelcaps and Tablets are used for the control of hyperphosphatemia (elevated serum phosphorus levels) in patients with end-stage renal (kidney) failure.
- O Nabi-HB® [Hepatitis B Immune Globulin (Human)] is a hyperimmune globulin used to treat patients acutely exposed to blood containing the hepatitis B virus (HBV).
- WinRho SDF® [Rho(D) Immune Globulin Intravenous (Human)] is a hyperimmune globulin used for the treatment of ITP, an autoimmune disorder affecting platelets.
- Aloprim™(Allopurinol sodium) for Injection is used for the management of patients with leukemia, lymphoma, and solid tumor malignancies who are receiving cancer therapy which causes elevations of serum and urinary uric acid levels and who cannot tolerate oral therapy.

Code No. 10340-00-GEN-130704

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* ABOUT US

+ PIPELINE

. PRODUCTS

OWERING THE IMM

HOME SEAR

PATIENTS

MEDIA

Hepatitis B Immune Globulin (Human)

Nabi-HB® (Hepatitis B Immune Globulin [Human]) is an immune globulin that contains antibodies to hepatitis B surface antigen (anti-HBs). In contrast to vaccination, which provides long-term immunity to hepatitis B, Nabi-HB provides passive immunization (i.e. short-term protection) following exposure to hepatitis B virus. Nabi-HB is indicated for the treatment of:

RESOURCES

Full Prescribing I Nabi-HB€

acute exposure to blood containing hepatitis B surface antigen (HBsAg)

Hepatitis B Reso

perinatal exposure of infants born to HBsAg-positive mothers

sexual exposure to HBsAg-positive persons

household exposure to persons with acute HBV infection.

Code No. 10570-42-HEP-150704

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The APLB Top Seven Problem List

- False information on approved indications and limitations of other marketed products
- 6. Promotion of broader indication than approved
- Promotion that product is more effective based on timing of drug administration in the absence of substantial evidence



The APLB Top Seven Problem List

- Omission of risk information
- Failure to submit materials to FDA
- Claims of "unsurpassed...safety"
- 4. Claims regarding the reduction in frequency or severity of adverse events or clinical symptoms in the absence of substantial evidence



Practical Advice

- When developing/approving promotional pieces:
 - ✓ Fair Balance risk information should be included in the body of the piece
 - ✓ It is not sufficient to simply attach the PI or the brief summary
 - ✓ Submit a copy to FDA at the same time you distribute the pieces



Corrective Actions

- ➤ <u>Warning letters</u> firms are requested to develop a plan of action to distribute corrective information to audience that received violative information
 - We have been consistent in this corrective action requirement
 - Because of the nature of the violation, the corrective message should be pro-active



Corrective Actions (cont'd)

Examples:

- Conferences send corrective letters to all conference attendees
- Journals send corrective letters to all subscribers or publish a corrective ad in journal(s)
- Website post correction on the website page(s)



Looking Ahead...

- ➤ Electronic Submission of 2253 Materials
- New guidance documents draft and final
- Continued vigorous enforcement
- Continue working interactively with industry to achieve voluntary compliance



Looking Ahead...

- ➤ Electronic submissions for FDA Form-2253 materials.
 - ✓ Similar to the January 2001 draft guidance on electronic submissions for ad/promo materials
 - ✓ Presently, we receive CDs with one paper 2253 from some companies instead of all paper
 - ✓ <u>Fully</u> electronic submissions through the CBER electronic document room within the year



Looking Ahead...

- Guidance Documents
 - ✓ Help-Seeking/Disease Awareness
 - ✓ Brief Summary Guidance
 - ✓ Outdoor Media
 - ✓ Presentation of Risk Information
 - ✓ Electronic Submissions



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www.fda.gov/cber/efoi/adpromo.htm